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Associations Between Obesity Indicators and Blood Pressure in Chinese Adult Twins

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Obesity is associated with blood pressure (BP), but the associations between different obesity indicators and BP have not reached agreement. Besides, both obesity and BP are influenced by genetic and environmental factors. Whether they share the same genetic or environmental etiology has not been fully understood. We therefore analyzed the relationship between different obesity indicators and BP components as well as the genetic and environmental contributions to these relationships in a Chinese adult twin sample. Twins aged 18–79 years ($n = 941$) were included in this study. Body mass index (BMI) was used as the index of general obesity, whereas waist circumference (WC), waist-to-height ratio (WHtR), and waist-to-hip ratio (WHR) were used as the indicators of central obesity. BP components included systolic blood pressure (SBP) and diastolic blood pressure (DBP). Linear regression models and bivariate structural equation models were used to examine the relation of various obesity indicators with BP components, and genetic or environmental influences on these associations, respectively. A strong association of BP components with BMI—and a somewhat weaker association with WC, WHtR, and WHR—was found in both sexes, independent of familial factors. Of these phenotypic correlations between obesity indicators and BP components, 60–76% were attributed to genetic factors, whereas 24–40% were attributed to unique environmental factors. General obesity was most strongly associated with high BP in Chinese adult twins. There were common genetic backgrounds for obesity and BP, and unique environmental factors also played a role.

■ **Keywords:** Chinese, obesity, blood pressure, genetic, adult, twin study

Hypertension is one of the most prevalent chronic medical conditions in China, with 29.6% Chinese adults having the condition (Wang et al., 2014). Hypertension represents a major public health challenge as it is considered to be the leading risk factor for cardiovascular mortality and accounts for a large proportion of premature deaths in China (Fang et al., 2014).

Obesity has been recognized as one of the most important risk factors for hypertension (Hall et al., 2015). Various anthropometric measures, such as the body mass index (BMI), waist circumference (WC), waist-to-height ratio (WHtR), and waist-to-hip ratio (WHR), have been proposed to define obesity. In recent years, emerging data have suggested that abdominal obesity is a more important risk factor for cardiovascular and metabolic diseases than is general obesity (Janssen et al., 2004). In most of the previous reports, the comparisons between these obesity indicators and hypertension have not reached an agreement, as some studies propose the use of central obesity indicators (Gus et al., 2004), whereas others have found them to be equivalent (Nyamdorj, Qiao, Lam, et al., 2008) or advocate their combined use (Lam et al., 2015).

Previous twin studies have shown that underlying continuous traits for both hypertension and obesity are significantly heritable. Heritability estimates for both systolic blood pressure (SBP) and diastolic blood pressure (DBP) are between 40% and 60% (Wang, Liao et al., 2015), and the heritability for obesity-related phenotypes is also

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substantial (Zhou et al., 2015). As most previous studies were unable to control for the individual genetic variability, it is therefore unknown whether the previous associations between obesity indicators and hypertension were attributable to shared genetic vulnerabilities influencing both phenotypes. Twin design is seen as a useful method of controlling confounders in observational epidemiologic studies. In particular, monozygotic (MZ) twins, who are completely matched for any variations in their genetic background, provide an extremely powerful control for genetic confounding factors. As such, comparing twins within pairs can provide a powerful control for genetic and shared environmental confounding factors that are typically different among unrelated individuals (McGue et al., 2010).

Several previous twin studies have shown that the association between blood pressure (BP) and obesity is independent of genetic factors (Newman et al., 1990), although other studies indicated the existence of a low–moderate common set of genetic and environmental backgrounds influencing both BMI and BP (Cui et al., 2002; Nelson et al., 2006; Wu et al., 2015). However, most of these studies focused on BMI as the indicator of obesity and were performed with Caucasian participants. Twin studies exploring the role of central fat accumulation, and in particular intra-abdominal or visceral fat deposits, in hypertension are rare.

Therefore, the purpose of this research was to examine the association of obesity indicators with BP components (SBP and DBP) using a sample of Chinese adult twins from the Chinese National Twin Registry (CNTR). Two specific obesity indicators were examined: (1) general obesity indicator (BMI) and (2) central obesity indicators (WC, WHtR, and WHR). Further, we extended the current study by estimating genetic and environmental contributions to the association of obesity indicators with SBP and DPB.

Methods

Study Sample

The participants belong to the CNTRwhich has been described previously (Li et al., 2013). During April–December 2013, a total of 1,147 subjects underwent a survey in Shandong, Zhejiang, Jiangsu, and Sichuan provinces. Twins were excluded from this study if they: (1) had a history of cancer, diabetes, cardiovascular heart disease, and stroke; (2) were being treated with medication affecting weight (e.g., insulin, thyroxin, and antipsychotic medication); (3) were without SBP or DBP measures. Finally, a total of 941 individuals (413 completed twin pairs and 115 individuals) were eligible for this study.

The determination of zygosity was based on age, gender, questions of appearance confused by strangers, and previously perceived zygosity from questionnaires. This method has been validated using DNA genotyping from 192 pairs of same-gender twins and found to have an AUC of 89.03% (Wang, Gao et al., 2015). All participants provided their written informed consent, and the Biomedical Ethics Committee at Peking University, Beijing, China approved the study protocol.

Physical Examination Measurements

Physical examinations were done in the same way in different sites, and all investigators were trained and qualified for measurements. Height was measured to the nearest 0.1 cm on a stadiometer, whereas weight was measured to the nearest 0.1 kg using a digital balance (Body Composition Analyzer/Scale, TANITA, Tokyo, Japan). BMI was calculated using the standard way: weight (kg)/height^2 (m). Waist and hip circumferences were measured to the nearest 0.1 cm using a standard tape with the subject in a standing position. WC was measured over the unclothed abdomen at the narrowest point between the costal margin and iliac crest, and hip circumference was measured over light clothing at the level of the widest diameter around the buttocks. WHR was calculated as WC (cm) divided by hip circumference (cm), whereas WHtR was calculated as WC (cm) divided by height (cm). Three consecutive BP readings were obtained after resting quietly in a seated position for 5 min by using a standard electronic sphygmomanometer with an interval of at least 30 s between measurements. The mean value of the three measurements was used in the analyses.

Assessment of Covariates

Covariates were obtained from questionnaire in this survey, including socio-demographic characteristics (age, sex, region, and socio-economic status (SES)) and lifestyle behaviors (tobacco smoking, alcohol drinking, and physical activity). Region was assessed by site of investigating (Shandong, Zhejiang, Jiangsu, and Sichuan province). SES was coded as low, medium, and high, as described in a previous study (Liao et al., 2015). Smoking was categorized as never smoking and ever smoking. Alcohol drinking status was similarly defined as never drinking and ever drinking. Self-reported salt-eating habit was recorded as low, medium, and high according to participants' responses to 'How salty do you usually eat your food?'. Participants' exercise activities in occupation, transportation, daily life, and leisure time were assigned a metabolic equivalent task (MET) value, using the Compendium of Physical Activities by Ainsworth et al. (2000).

Statistical Methods

Gender-specific descriptive analyses were used to examine sample differences in study covariates, obesity indicators, and BP components; p values were corrected for the correlation between co-twins.

Phenotypic correlations between the traits were made either between individuals or between co-twins in a pair. Co-twin differences of obesity-related measures were calculated for each twin pair and the biochemical variables

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by using the difference of log-transformed values (co-twin difference = twin1− twin2), which are defined by birth order. Spearman rank correlations were used to examine the relation between these measures. To determine the population (between-individual) effects, we used a sex-specific, mixed-effect linear regression model with a random intercept for each twin pair to account for twin clustering (Carlin et al., 2005) in the entire sample, treating twins as individuals to examine the relationship between obesity indicators and BP components. Further, to investigate whether these associations were confounded by familial factors, we applied co-twin regression analyses within MZ twin pairs with R^2 values calculated. The within-pair approach automatically takes into account shared genetic and environmental influences. In order to make a comparison between effects of different obesity indicators on BP components, we standardized all the obesity indicators into *z* scores for each linear regression model. A *z* score was calculated for each measurement as the observed value minus the mean value, divided by the standard deviation within each stratum of age and gender group (Wang et al., 2007). We also explored effect modification of the obesity–BP relationship by gender. All models were adjusted for age, zygosity, region, SES, smoking status, drinking status, salt-eating habit, and MET value.

Both SBP and DBP were handled after logarithmic transformation in the regression analyses. Robust standard error and confidence intervals for estimates have been produced. All the statistical analyses were performed with Stata statistical software (release 12.0; Stata Corporation, College Station, TX). *P* values were two-sided, and statistical significance was assumed at $p < .05$.

A structural equation model was used to examine the extent to which genetic or environmental variance were correlated across obesity indicators and BP components. At first, intraclass correlation coefficients (ICCs) were calculated. For genetic analyses, we fitted a univariate structural equation model to separate the observed phenotypic variance into its genetic and environmental components: additive (A) genetic components and common (C) or unique (E) environmental components. A nested model for which A or C was equated to zero was also fitted, and Akaike Information Criterion (AIC) was used for comparison of goodness of fit of the models. Next, based on the best-fit model, we fitted the bivariate Cholesky decomposition models to calculate genetic (r_G) and environmental correlations (r_E) between obesity indicators and BP components and 95% CIs. All model-fitting analyses and maximum-likelihood parameter estimates were performed in OpenMx (Version 1.4) with log-transformed BP components and *z*-scored data of obesity indicators among same-sex twin pairs. All variance components of obesity indicators were estimated with inclusion of age, sex, region, SES, smoking status, and drinking status as covariates, whereas variance components of BP measures were additionally adjusted for salt-eating habit in the models. MET value was not included because of 55 missing values.

Results

Sample Characteristics

A total of 941 individuals, including 248 complete MZ twin pairs and 165 complete dizygotic (DZ) twin pairs, were included in this study, of which 65% were male twins. The distribution of epidemiological and physical characteristics by gender is given in Table 1. In general, men and women did not differ in age and SES. Compared with men, women smoked less, consumed less alcohol, got less physical activity, and were less likely to have a salty taste ($p < .05$ for all comparisons). With respect to physical indicators, men were heavier and had a larger WC and WHR than those of women ($p < .001$ for all comparisons). SBPs and DBPs were also significantly higher in men than in women ($p < .001$).

Associations of Obesity Indicators with BP Components

Spearman rank correlations between the measures of obesity and BP were analyzed for each individual separately and within twin pairs (Table 2). After twin-pair normalization, that is, after controlling for genetic factors, the positive correlations of BMI, WC, and WHtR with SBP and DBP became more pronounced than the correlations performed in individual subjects.

The results of multiple regression models examining the associations of obesity indicators with BP components in the whole twin sample as well as within MZ twin pairs are presented in Tables 3 and 4. In the whole sample, treating twins as individuals, a positive relationship was observed between obesity indicators and BP components in both genders (Table 3). In further analyses controlling for familial factors within 248 MZ twin pairs, obesity indicators still exerted significant associations with BP components (Table 4). In order to compare the strength of the association for various obesity indicators in relation to BP components, we further standardized all the obesity indicators into *z* scores and performed similar linear regression within MZ twin pairs. As shown in the bottom of Table 4, there existed a stronger positive correlation of BP components with BMI than with other measures of obesity. The proportion of the variance in the levels of BP components explained by obesity indicators varied (6–11%), and obesity indicators in our models with larger β coefficients had relatively higher R^2 values, accounting for more variability of the BP components. Among these obesity measurements, BMI explained the highest variance in both SBP and DBP levels, whereas WHR explained the lowest variance in levels of SBP and DBP. Tests for statistically difference in association of different measures of obesity with BP components between male and female MZ twins supported a sex-specific role of BMI on DBP (BMI-by-sex interaction, $p = .037$, Supplementary

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TABLE 1

Epidemiological and Physical Characteristics of the 941 Chinese Adult Twins

	All twins ($n = 941$)	Male twins ($n = 612$)	Female twins ($n = 329$)	p value[a]
Epidemiological characteristics				
Age (years), mean (*SD*)	45.4 (13.0)	45.9(12.6)	44.2(13.7)	.814
Zgosity (MZ), *n* (%)	568 (60.4)	373 (60.9)	195 (59.3)	.715
Region, *n* (%)				
Qingdao	188 (20.0)	142 (23.2)	46 (14.0)	.002
Jiangsu	365 (38.8)	218 (35.6)	147 (44.7)	
Sichuan	103 (10.9)	72 (11.8)	31 (9.4)	
Zhejiang	285 (30.3)	180 (29.4)	105 (31.9)	
SES, *n* (%)				
Low	196 (20.8)	126 (20.6)	70 (21.3)	.352
Medium	660 (70.1)	425 (69.4)	235 (71.4)	
High	83 (8.8)	60 (9.8)	23 (7.0)	
Smoking status, *n* (%)				
Never	534 (56.7)	209 (34.2)	325 (98.8)	<.001
Ever	400 (42.5)	398 (65.0)	2 (0.6)	
Drinking status, *n* (%)				
Never	598 (63.5)	306 (50.0)	292 (88.8)	<.001
Ever	337 (35.8)	301 (49.2)	36 (10.9)	
Salt-eating habit, *n* (%)				
Low	308 (32.7)	182 (29.7)	126 (38.3)	.024
Medium	281 (29.9)	187 (30.6)	94 (28.6)	
High	351 (37.3)	242 (39.5)	109 (33.1)	
MET value, median (range)[b]	5,148 (46, 815)	6,438 (46, 815)	4,410 (30, 351)	<.001
Physical characteristics, median (interquartile range)				
BMI (kg/m^2)	24.4 (21.9, 26.8)	24.9 (22.4, 27.1)	23.3 (20.9, 25.8)	<.001
WC (cm)	86.0 (78.3, 93.0)	88.9 (82.0, 94.5)	82.0 (74.5, 88.0)	<.001
WHtR	0.53 (0.49, 0.57)	0.54 (0.49, 0.57)	0.53 (0.48, 0.57)	.182
WHR	0.90 (0.85, 0.94)	0.91 (0.87, 0.95)	0.86 (0.82, 0.90)	<.001
SBP (mmHg)	131.0 (120.5, 145.7)	133.0 (123.1, 147.6)	126.5 (112.0, 140.8)	<.001
DBP (mmHg)	79.5 (72.0, 87.3)	81.5 (74.0, 89.0)	75.7 (68.5, 84.0)	<.001

Note: *SD* = standard deviation; MZ = monozygotic; SES = socio-economic status; MET value = metabolic equivalent value; BMI = body mass index; WC = waist circumference; WHtR = waist–height ratio; WHR = waist–hip ratio, SBP = systolic blood pressure; DBP = diastolic blood pressure. *N* = 941 individuals (413 twin pairs and 115 individuals) and percentage may not sum to total due to missing values.

[a] *p* values were corrected for the correlation between co-twins.

[b] MET values were available for 886 individuals.

TABLE 2

Spearman Rank Correlations Between Obesity-Related Measures and Blood Pressure

	SBP	DBP	BMI	WC	WHtR
Individual ($n = 941$).					
DBP	0.769 (0.737, 0.800)				
BMI	0.252 (0.191, 0.313)	0.325 (0.263, 0.382)			
WC	0.298 (0.237, 0.357)	0.353 (0.300, 0.410)	0.852 (0.829, 0.872)		
WHtR	0.283 (0.223, 0.336)	0.302 (0.244, 0.358)	0.812 (0.785, 0.836)	0.894 (0.878, 0.907)	
WHR	0.285 (0.222, 0.340)	0.335 (0.278, 0.391)	0.617 (0.573, 0.658)	0.811 (0.781, 0.835)	0.785 (0.751, 0.812)
Twin-normalized ($n = 413$)					
DBP	0.704 (0.643, 0.759)				
BMI	0.370 (0.283, 0.454)	0.386 (0.296, 0.476)			
WC	0.322 (0.236, 0.414)	0.363 (0.271, 0.445)	0.847 (0.798, 0.888)		
WHtR	0.311 (0.219, 0.402)	0.345 (0.252, 0.428)	0.851 (0.807, 0.888)	0.959 (0.944, 0.970)	
WHR	0.210 (0.115, 0.300)	0.282 (0.187, 0.365)	0.591 (0.515, 0.658)	0.798 (0.748, 0.841)	0.779 (0.716, 0.827)

Note: SBP = systolic blood pressure; DBP = diastolic blood pressure; BMI = body mass index; WC = waist circumference; WHtR = waist–height ratio; WHR = waist–hip ratio.

Table 1). Stratified analyses by sex were slightly hampered by reduced statistical power. Nevertheless, the same pattern of associations was obvious within MZ male twins but not within MZ female twins (Supplementary Table 1).

Genetic and Environmental Contributions to the Obesity–BP Associations

The obesity indicators and BP components were all traits influenced by genetic factors. This was reflected by a higher ICC in MZ twins than in DZ twins (Supplementary Table 2). We first fitted a saturated model (ACE model) that allowed for additive genetic (A), common environmental (C), and unique environmental (E) components for each obesity indicator and BP component. We also fitted alternative models for which A, C, and E were equated to zero, that is, CE, AE, and AC models, respectively. Chi-square and AICs were used for comparison of goodness of fit of the models. We presented the estimates from the best-fitted models that

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TABLE 3

Random-Intercept Regression Analyses of Obesity-Related Measures With BP Components in 941 Chinese Adult Twins Stratified By Gender

	SBP (mmol/L) β [95% CI]	DBP (mmol/L) β [95% CI]
Male twins		
BMI (kg/m^2)	0.012 [0.009, 0.015]***	0.016 [0.013, 0.019]***
WC (cm)	0.003 [0.002, 0.004]***	0.004 [0.003, 0.006]***
WHtR	0.502 [0.330, 0.674]***	0.674 [0.491, 0.856]***
WHR	0.235 [0.086, 0.385]***	0.433 [0.274, 0.592]***
Female twins		
BMI (kg/m^2)	0.010 [0.006, 0.014]***	0.010 [0.006, 0.014]***
WC (cm)	0.003 [0.002, 0.005]***	0.003 [0.002, 0.005]***
WHtR	0.516 [0.279, 0.754]***	0.504 [0.274, 0.735]***
WHR	0.458 [0.202, 0.714]***	0.456 [0.207, 0.705]***

Note: BP = blood pressure; SBP = systolic blood pressure; DBP = diastolic blood pressure; BMI = body mass index; WC = waist circumference; WHtR = waist–height ratio; WHR = waist–hip ratio.
All regression models were adjusted for age, zygosity, region, socioeconomic status, smoking status, drinking status, salt-eating habit, and MET value.
*$p < .05$, **$p < .01$, ***$p < .001$.

had the lowest AIC and did not have a significantly worse fit compared with the saturated model (i.e., chi-square test, p value $>.05$). The additive genetic/unique environment (AE) model offered the best fit for all traits, and the results can be seen in Supplementary Table 3. In general, after multiple adjustments, the estimate of heritability was 60.9% for SBP and 63.5% for DBP. For obesity-related measures, heritability was estimated lowest for WHR at 44.5%, whereas it was highest for BMI at 63.0%.

The bivariate Cholesky decomposition models were then used to decompose phenotypic correlation into additive genetic and unique environmental correlations. The results revealed high genetic correlation between SBP and DBP, and low–moderate genetic association of BMI and WC with SBP and DBP, as well as WHtR and WHR with DBP. Significant unique environmental effects also contributed to these relationships. Among these phenotype pairs, 60–76% of the total phenotypic correlations between each phenotype pair were determined by genetic factors, whereas the remaining 24–40% were explained by unique environmental factors in this Chinese adult twin sample (Table 5).

Discussion

This study on a sample of Chinese adult twins showed a strong association of BP components with BMI, and a somewhat weaker association with WC, WHtR, and WHR when using within-pair analyses in MZ twins. To a large degree, shared genetic factors contributed to these associations, with the remaining explained by unique environmental factors.

Obesity has been well known as a risk factor for hypertension, but it is still unclear whether this risk can better estimated by general obesity measures or central obesity measures. The regression analyses showed that there were significant associations between obesity indicators and BP components in all twins. When controlling for familial factors using MZ twins, BMI had a stronger association with BP components than central obesity indicators in both sexes. In a meta-analyses study of Asians (Nyamdorj, Qiao, Lam, et al., 2008), hypertension had a stronger association with BMI than central obesity measures in both men and women, which supported our findings. In several other previous studies, compared with other adiposity indices, BMI had a stronger association with SBP and DBP in Chinese children and adolescents (Wang et al., 2008), in Mauritian Indian women (Nyamdorj, Qiao, Soderberg, et al., 2008), in Japanese women (Sakurai et al., 2006), and in men in the United States (Roka et al., 2015). These results are similar to ours, but some found gender differences in the association between various obesity-related measures and BP (Sakurai et al., 2006; Roka et al., 2015) that was not found in this study. The observed differences between these studies and our study may be explained by differences in the study population, study design, and sample size, as well as by differences in adjustments. Analyses stratified by sex revealed that increasing BMI exerted a sex-specific deleterious role on DBP, being stronger within MZ male twins than within MZ female twins, which needs to be replicated in other studies.

In keeping with earlier twin studies (Maes et al., 1997; Schousboe et al., 2003; Zhou et al., 2015), the overall heritability estimates for obesity indicators and BP components were moderate to high, ranging from 44.5% to 63.5%. These results indicated that this phenotypic variation was largely due to genetic effects. By decomposing phenotypic correlation into additive genetic and unique environmental correlations, the variable estimates by Cholesky decomposition further revealed that the phenotype correlation among obesity indicators and BP components had genetic backgrounds. A genetic correlation of 1.0 would indicate that genetic influences on the two traits completely overlap, whereas a genetic correlation of zero would indicate that entirely different genes influence the two traits (Y. Wu et al., 2015). We found high genetic correlations between SBP and DBP, indicating that genes identified as affecting SBP may overlap with those associated with DBP. This opinion has been supported by a recent BP genome-wide association study (Ehret et al., 2011), which has found that 29 independent SNPs at 28 loci were significantly associated with both SBP and DBP. On the contrary, the estimate of genetic association of obesity indicators with BP components was much weaker but still significant, and the results of genetic correlation between BMI and SBP as well as DBP were close to the results of another two Chinese twin studies (Wu et al., 2011; Wu et al., 2015). In addition, genetic contribution to observed phenotypic correlation was also calculated for these phenotype pairs. A high genetic correlation may not always mean that genes contribute largely to the observed correlation, whereas a high genetic

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TABLE 4

Fixed-Effect Regression Analyses of Obesity-Related Measures With BP Components Within 248 MZ Twin Pairs, Genders Combined

	SBP (mmol/L)		DBP (mmol/L)	
	β [95% CI]	R^2	B [95% CI]	R^2
BMI (kg/m^2)	0.010 [0.004, 0.015]***	0.100	0.010 [0.005, 0.016]***	0.096
WC (cm)	0.003 [0.001, 0.005]**	0.096	0.003 [0.001, 0.004]**	0.075
WHtR	0.491 [0.233, 0.749]***	0.097	0.429 [0.156, 0.702]**	0.074
WHR	0.219 [0.002, 0.435]*	0.060	0.271 [0.036, 0.506]*	0.057
ZBMI	0.034 [0.016, 0.052]***	0.107	0.039 [0.022, 0.056]***	0.109
ZWC	0.027 [0.012, 0.042]**	0.089	0.029 [0.013, 0.045]**	0.085
ZWHtR	0.027 [0.011, 0.043]**	0.086	0.030 [0.013, 0.047]**	0.083
ZWHR	0.014 [0.001, 0.027]*	0.061	0.017 [0.003, 0.032]*	0.059

Note: BP = blood pressure; SBP = systolic blood pressure; DBP = diastolic blood pressure; BMI = body mass index; WC = waist circumference; WHtR = waist–height ratio; WHR = waist–hip ratio. ZBMI = *z* score of BMI; ZWC = *z* score of WC; ZWHtR = *z* score of WHtR; ZWHR = *z* score of WHR. All regression models were adjusted for age, sex, region, socio-economic status, smoking status, drinking status, salt-eating habit, and MET value.
*$p < .05$, **$p < .01$, ***$p < .001$.

TABLE 5

Bivariate Genetic Analyses of the Estimated Genetic and Environmental Correlation Coefficients for Phenotype Pairs

Phenotype	r_G [95% CI]	r_E [95% CI]	c_G	c_E	r_P	%$_G$[a]	%$_E$[a]
SBP-DBP	0.764 [0.578, 0.827]	0.721 [0.656, 0.777]	0.48	0.27	0.75	63.56	36.44
BMI-SBP	0.310 [0.071, 0.640]	0.273 [0.149, 0.387]	0.19	0.10	0.29	64.90	35.10
WC-SBP	0.309 [0.046, 0.656]	0.204 [0.081, 0.321]	0.18	0.08	0.26	69.18	30.82
WHtR-SBP	0.317 [-0.017, 0.712]	0.192 [0.068, 0.309]	0.19	0.08	0.27	–	–
WHR-SBP	0.377 [-0.091, 1.000]	0.085 [-0.040, 0.207]	0.20	0.04	0.24	–	–
BMI-DBP	0.369 [0.145, 0.678]	0.311 [0.192, 0.421]	0.23	0.11	0.34	67.13	32.87
WC-DBP	0.374 [0.128, 0.722]	0.253 [0.131, 0.366]	0.23	0.10	0.33	69.83	30.17
WHtR-DBP	0.392 [0.079, 0.780]	0.250 [0.129, 0.363]	0.15	0.10	0.25	60.34	39.66
WHR-DBP	0.457 [0.031, 1.000]	0.169 [0.045, 0.287]	0.24	0.08	0.32	76.16	23.84

Note: $n = 242$ monozygotic and 105 dizygotic twin pairs. r_G = genetic correlation between two phenotypes; r_E = unique environmental correlation between two phenotypes; c_G and c_E = genetic and unique environmental contributions to the correlation between two phenotypes, respectively; $c_G = r_G * \sqrt{A_1 * A_2}$; $c_E = r_E * \sqrt{E_1 * E_2}$; $r_P = r_G * \sqrt{A_1 * A_2} + r_E * \sqrt{E_1 * E_2}$; %$_G$ and %$_E$ = percentage of genetic and unique environmental contributions to the correlation between two phenotypes. SBP = systolic blood pressure; DBP = diastolic blood pressure; BMI = body mass index; WC = waist circumference; WHtR = waist–height ratio; WHR = waist–hip ratio.
Models were adjusted for age, sex, region, socio-economic status, smoking status, and drinking status for variance component of obesity-related measures, while additionally adjusted for salt intake for variance component of SBP and DBP.
[a]%$_G$ and %$_E$ were only calculated in phenotype pairs with significant r_G and r_E.

contribution to observed phenotypic correlation would suggest that phenotypic correlation between the traits is largely due to genetic effects. In this study, a large genetic contribution to phenotypic correlations was found among obesity indicators and BP components (60–76%), which was consistent with the results obtained by Choh et al. (2001) in American Samoan families, as well as by Duan et al. (2011) in Chinese Qingdao twin samples. In one early study of the phenomenon, data on 2,508 adult male twins have suggested the presence of a common underlying factor mediating the clustering of hypertension and obesity, of which 59% was contributed by genetic factors (Carmelli et al., 1994). Recently, a study showed that there were genomic regions exerting pleiotropic effects on obesity and cardiovascular disease risk factors (Rankinen et al., 2015), which supported our findings.

Unique environmental factors also contributed to the associations between obesity indicators and BP components. This observation was in line with our previous regression analyses in identical twins, as well as another twin study (Newman et al., 1990), which showed that obesity was associated with BP independent of genetic background. Previous studies also showed that the environmental factors influenced the clustering of hypertension, and obesity appeared to be specific rather than shared by co-twins (Carmelli et al., 1994). Since obesity-related, non-genetic factors played a significant contribution to higher BP, there is a potential for obesity-related comorbidities prevention through modification of environmental factors. Taken together, both genetic and unique environmental factors explained the associations between obesity indicators and BP components, among which additive genetic correlations were stronger than unique environmental correlations.

This is the first study conducted in China using a sample of adult twins to evaluate and compare the association between various obesity indicators and BP components adjusting for multiple lifestyle factors. However, this study is not without its limitations. First, obesity indicators are all

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surrogate measures of obesity, and a more direct and accurate assessment of adiposity measured by dual-energy X-ray absorptiometry (DXA) or computed tomography (CT) may be less error-prone; however, studies have observed the discriminatory capability of those simpler measures to be equal to or even more robust than the measures derived from DXA or CT in prediction of metabolic syndrome or visceral fat (Beydoun et al., 2011; Soto et al., 2007). In addition, salt-eating habit was used as a surrogate measure of salt intake of the subjects in the analyses, which might be inaccurate. However, studies have found that the self-reported salt-eating habit had the ability to predict actual salt intake in adults (Lee et al., 2014). Second, as we had no detailed information on energy intake, the possibility of residual confounding by the unmeasured covariates cannot be excluded. Third, although our current sample size allowed us to demonstrate an association between obesity-related measures and BP components, an even larger sample size would be required to detect more subtle associations. Finally, this study is a cross-sectional study; thus, causality cannot be drawn from the association observed.

In summary, using a twin design to better control for confounders, we observed different associations between obesity indicators and BP components and demonstrated that BMI associated with BP components better than other central obesity measures. Of these phenotypic correlations, 60–76% was attributed to genetic factors, whereas the remaining 24–40% was attributed to unique environmental factors. As genetic factors explained a large proportion of obesity–BP relation, further studies are needed to determine specific genes that influence both obesity-related measures and BP components. Furthermore, prospective studies using a larger sample, preferably with direct measures of visceral obesity and detailed information on energy intake, are required to determine whether the direct measures will provide more information above and beyond surrogate measures of central obesity in the prediction of high BP.

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Supplementary Material

To view supplementary material for this article, please visit https://doi.org/10.1017/thg.2016.95.

References

Ainsworth, B. E., Haskell, W. L., Whitt, M. C., Irwin, M. L., Swartz, A. M., Strath, S. J., … Leon, A. S. (2000). Compendium of physical activities: An update of activity codes and MET intensities. *Medicine & Science in Sports & Exercise, 32*, S498–S504.

Beydoun, M. A., Kuczmarski, M. T., Wang, Y., Mason, M. A., Evans, M. K., & Zonderman, A. B. (2011). Receiver-operating characteristics of adiposity for metabolic syndrome: The healthy aging in neighborhoods of diversity across the life span (HANDLS) study. *Public Health Nutrition*, *14*, 77–92.

Carlin, J. B., Gurrin, L. C., Sterne, J. A., Morley, R., & Dwyer, T. (2005). Regression models for twin studies: A critical review. *International Journal of Epidemiology, 34*, 1089–1099.

Carmelli, D., Cardon, L. R., & Fabsitz, R. (1994). Clustering of hypertension, diabetes, and obesity in adult male twins: Same genes or same environments? *American Journal of Human Genetics, 55*, 566–573.

Choh, A. C., Gage, T. B., McGarvey, S. T., & Comuzzie, A. G. (2001). Genetic and environmental correlations between various anthropometric and blood pressure traits among adult Samoans. *American Journal of Physical Anthropology*, *115*, 304–311.

Cui, J., Hopper, J. L., & Harrap, S. B. (2002). Genes and family environment explain correlations between blood pressure and body mass index. *Hypertension, 40*, 7–12.

Duan, H., Pang, Z., Zhang, D., Li, S., Kruse, T. A., Kyvik, K. O., … Tan, Q. (2011). Genetic and environmental dissections of sub-phenotypes of metabolic syndrome in the Chinese population: A twin-based heritability study. *Obesity Facts, 4*, 99–104.

Ehret, G. B., Munroe, P. B., Rice, K. M., Bochud, M., Johnson, A. D., Chasman, D. I., … Johnson, T. (2011). Genetic variants in novel pathways influence blood pressure and cardiovascular disease risk. *Nature, 478*, 103–109.

Fang, L., Song, J., Ma, Z., Zhang, L., Jing, C., & Chen, D. (2014). Prevalence and characteristics of hypertension in mainland Chinese adults over decades: A systematic review. *Journal of Human Hypertension, 28*, 649–656.

Gus, M., Fuchs, S. C., Moreira, L. B., Moraes, R. S., Wiehe, M., Silva, A. F., … Fuchs, F. D. (2004). Association between different measurements of obesity and the incidence of hypertension. *American Journal of Hypertension, 17*, 50–53.

Hall, J. E., Do, C. J., Da, S. A., Wang, Z., & Hall, M. E. (2015). Obesity-induced hypertension: Interaction of neurohumoral and renal mechanisms. *Circulation Research, 116*, 991–1006.

Janssen, I., Katzmarzyk, P. T., & Ross, R. (2004). Waist circumference and not body mass index explains obesity-related health risk. *The American Journal of Clinical Nutrition, 79*, 379–384.

Lam, B. C., Koh, G. C., Chen, C., Wong, M. T., & Fallows, S. J. (2015). Comparison of body mass index (BMI), body adiposity index (BAI), waist circumference (WC), waist-to-hip ratio (WHR) and waist-to-height ratio (WHtR) as predictors of cardiovascular disease risk factors in an adult population in Singapore. *PLoS One, 10*, e122985.

Lee, H., Cho, H. J., Bae, E., Kim, Y. C., Kim, S., & Chin, H. J. (2014). Not salt taste perception but self-reported salt eating habit predicts actual salt intake. *Journal of Korean Medical Science*, *29*, S91–S96.

Li, L., Gao, W., Yu, C., Lv, J., Cao, W., Zhan, S., … Hu, Y. (2013). The Chinese national twin registry: An update. *Twin Research and Human Genetics, 16*, 86–90.

Liao, C., Gao, W., Cao, W., Lv, J., Yu, C., Wang, S., … Li, L. (2015). Associations of body composition measurements with serum lipid, glucose and insulin profile: A Chinese twin study. *PLoS One, 10*, e140595.

Maes, H. H., Neale, M. C., & Eaves, L. J. (1997). Genetic and environmental factors in relative body weight and human adiposity. *Behavior Genetics, 27*, 325–351.

McGue, M., Osler, M., & Christensen, K. (2010). Causal inference and observational research: The utility of twins. *Perspectives on Psychological Science, 5*, 546–556.

Nelson, T. L., Brandon, D. T., Wiggins, S. A., & Whitfield, K. E. (2006). Genetic and environmental influences on body fat and blood pressure in African-American adult twins. *International Journal of Obesity*, *30*, 243–250.

Newman, B., Selby, J. V., Quesenberry, C. J., King, M. C., Friedman, G. D., & Fabsitz, R. R. (1990). Nongenetic influences of obesity on other cardiovascular disease risk factors: An analysis of identical twins. *American Journal of Public Health, 80*, 675–678.

Nyamdorj, R., Qiao, Q., Lam, T. H., Tuomilehto, J., Ho, S. Y., Pitkaniemi, J., … Ferreira, S. R. (2008). BMI compared with central obesity indicators in relation to diabetes and hypertension in Asians. *Obesity (Silver Spring), 16*, 1622–1635.

Nyamdorj, R., Qiao, Q., Soderberg, S., Pitkaniemi, J., Zimmet, P., Shaw, J., … Tuomilehto, J. (2008). Comparison of body mass index with waist circumference, waist-to-hip ratio, and waist-to-stature ratio as a predictor of hypertension incidence in Mauritius. *Journal of Hypertension, 26*, 866–870.

Rankinen, T., Sarzynski, M. A., Ghosh, S., & Bouchard, C. (2015). Are there genetic paths common to obesity,cardiovascular disease outcomes, and cardiovascular risk factors? *Circulation Research, 116*, 909–922.

Roka, R., Michimi, A., & Macy, G. (2015). Associations between hypertension and body mass index and waist circumference in U.S. adults: A comparative analysis by gender. *High Blood Pressure & Cardiovascular Prevention, 22*, 265–273.

Sakurai, M., Miura, K., Takamura, T., Ota, T., Ishizaki, M., Morikawa, Y., … Nakagawa, H. (2006). Gender differences in the association between anthropometric indices of obesity and blood pressure in Japanese. *Hypertension Research, 29*, 75–80.

Schousboe, K., Willemsen, G., Kyvik, K. O., Mortensen, J., Boomsma, D. I., Cornes, B. K., … Kaprio, J. (2003). Sex differences in heritability of BMI: A comparative study of results from twin studies in eight countries. *Twin Research, 6*, 409–421.

Soto, G. A., Bellido, D., Buno, M. M., Pertega, S., De Luis, D., Martinez-Olmos, M., & Vidal, O. (2007). Predictors of the metabolic syndrome and correlation with computed axial tomography. *Nutrition, 23*, 36–45.

Wang, B., Gao, W., Yu, C., Cao, W., Lv, J., Wang, S., … Li, L. (2015). Determination of zygosity in adult Chinese twins using the 450K methylation array versus questionnaire data. *PLoS One, 10*, e123992.

Wang, B., Liao, C., Zhou, B., Cao, W., Lv, J., Yu, C., … Li, L. (2015). Genetic contribution to the variance of blood pressure and heart rate: A systematic review and meta-regression of twin studies. *Twin Research and Human Genetics, 18*, 158–170.

Wang, H., Necheles, J., Carnethon, M., Wang, B., Li, Z., Wang, L., … Wang, X. (2008). Adiposity measures and blood pressure in Chinese children and adolescents. *Archives of Disease in Childhood, 93*, 738–744.

Wang, B., Necheles, J., Ouyang, F., Ma, W., Li, Z., Liu, X., … Wang, X. (2007). Monozygotic co-twin analyses of body composition measurements and serum lipids. *Preventive Medicine, 45*, 358–365.

Wang, J., Zhang, L., Wang, F., Liu, L., & Wang, H. (2014). Prevalence, awareness, treatment, and control of hypertension in China: Results from a national survey. *American Journal of Hypertension, 27*, 1355–1361.

Wu, T., Snieder, H., Li, L., Cao, W., Zhan, S., Lv, J., … Hu, Y. (2011). Genetic and environmental influences on blood pressure and body mass index in Han Chinese: A twin study. *Hypertension Research, 34*, 173–179.

Wu, Y., Zhang, D., Pang, Z., Jiang, W., Wang, S., Li, S., … Tan, Q. (2015). Multivariate modeling of body mass index, pulse pressure, systolic and diastolic blood pressure in Chinese twins. *Twin Research and Human Genetics, 18*, 73–78.

Zhou, B., Gao, W., Lv, J., Yu, C., Wang, S., Liao, C., … Li, L. (2015). Genetic and environmental influences on obesity-related phenotypes in Chinese twins reared apart and together. *Behavior Genetics, 45*, 427–437.

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